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Copper-catalyzed synthesis of sulfonamides from nitroarenes with the insertion of sulfur dioxide

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Nitroarenes are used as the coupling partner in the preparation of sulfonamides via the insertion of sulfur dioxide. A three-component reaction of arylboronic acids, nitroarenes, and potassium metabisulfite under copper catalysis proceeds smoothly, giving rise to a range of sulfonamides in good to excellent yields with broad substrate scope. Various functional groups including hydroxyl, cyano, amino, and carbonyl are all tolerated. A plausible mechanism is proposed, showing that arylsulfinate is the intermediate and the copper-assisted interaction of nitroarene and arylsulfinate is the key step. This approach is also extended to the late-stage modification of current marketed drug (Flutamide).

It is known that nitroarenes are basic raw chemical materials, which are well applied in the fields of pharmaceuticals, pesticide, and dye industries. They can be easily accessed through the nitration of arenes.[1] So far, the applications of nitroarenes have been extensively explored in synthetic chemistry. For instance, the Sandmeyer-type reactions of anilines originated from nitroarenes could afford many functionalized haloarenes. Recently, using nitroarenes as the aryl sources in metal-catalyzed cross-coupling reactions were developed as well, although the inertness of C–N bond toward oxidative addition hampered its further development.[2] For example, synthesis of aromatic ethers through C–O coupling of electron-deficient nitroarenes and arylboronic acids by using rhodium or nano-sized copper catalyst was described.[3] Nakao and co-workers reported the hydrodenitration, Suzuki coupling, and Buchwald–Hartwig amination of nitroarenes under palladium catalysis by using Buchwald biaryl monophosphines (BrettPhos) as the ligand.[4] Chen and co-workers disclosed the preparation of diarylamines and N-alkylanilines via a palladium/NHC-catalyzed dinitrative C–N coupling of nitroarenes and amines.[5]

A recent focus of our laboratory has been centred on the synthesis of sulfonyl-containing compounds through the insertion of sulfur dioxide by using DABCO·$(SO_2)_2$[6] or potassium/sodium metabisulfite.[7,8] Since sulfonamides are broadly found in pharmaceuticals and agrochemicals,[9] we conceived that the insertion of sulfur dioxide and the application of nitroarenes could be combined, which would provide a rapid access to sulfonamides.

In the past few years, incorporation of sulfonyl unit into small molecules via the insertion of sulfur dioxide under metal catalysis or through radical process has developed.[10,11] For example, we disclosed a palladium-catalyzed three-component coupling of arylboronic acids, sulfur dioxide and hydrazines,[11a] and subsequently reported the first example by using potassium metabisulfite as the source of sulfur dioxide.[11b] Sulfonamides could also be obtained via a one-pot process through a reaction of aryldiazonium tetrafluoroborates, DABCO·$(SO_2)_2$ and amines in the presence of N-hydroxybenzotrizole,[11c] or through a copper-catalyzed aminosulfonylation of aryldiazonium tetrafluoroborates, DABCO·$(SO_2)_2$ and N-chloroamines.[11d] Willis and co-workers described a copper-catalyzed three-component synthesis of sulfonamides from arylboronic acids at high temerpature.[11e] Jiang and co-workers reported the construction of primary sulfonamides through a reaction of aryldiazonium tetrafluoroborates, sodium metabisulfite and sodium azide in the presence of large excess amount of triphenylphosphine.[11f] Synthesis of sulfonamides through a copper-catalyzed reaction of triarylbismuthines, sodium metabisulfite, and nitro compounds was developed by using deep eutectic solvent as a reaction medium, as reported by Guillena and J. Ramón.[11g] This is a breakthrough for the transformation of nitroarenes, which combine with sulfur dioxide under copper catalysis. Encouraged by these results and prompted by the recent progress for the metal-catalyzed cross-coupling reactions of nitroarenes, we envisioned that nitroarenes might be used as the coupling partner with arylboronic acids in the preparation of sulfonamides via the insertion of sulfur dioxide. Herein, we report a three-component reaction of arylboronic acids, nitroarenes, and potassium metabisulfite under copper catalysis, giving rise to a range of sulfonamides in good to excellent yields with broad substrate scope. Various functional groups including hydroxyl, cyano, amino, and carbonyl are all tolerated. A plausible mechanism is proposed, showing arylsulfinate is the intermediate and the copper-assisted interaction of nitroarene and arylsulfinate is the key step.

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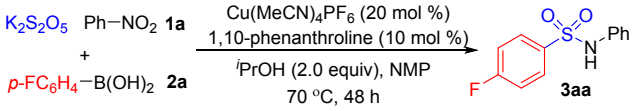
At the outset, nitrobenzene **1a** and 4-fluorobenzeneboronic acid **2a** were selected as model substrates for reaction development. After careful optimization of the reaction conditions (see SI for details), a "standard condition" was established (Table 1). The corresponding product of 4-fluoro-*N*-phenylbenzenesulfonamide **3aa** was obtained and isolated in 77% yield with $Cu(MeCN)_4PF_6$ as catalyst and 1,10-phenanthroline as ligand (Table 1, entry 1). The reaction could not proceed without the addition of copper catalyst (Table 1, entry 2). It should be noted that the loading amount of the ligand was the half of copper catalyst, since either increasing and decreasing the ligand dosage would make the reaction less effective (Table 1, entries 3 and 4). Reducing the catalyst loading also led to inferior results (Table 1, entry 5). During the investigation of the impact of different copper catalysts, the addition of $Cu(MeCN)_4PF_6$ gave the best result while reactions with other copper catalysts showed lower yields (Table 1, entries 6 and 7). Moreover, isopropanol was employed as the reductant in the coupling reaction because of its low cost and ease of separation. The reaction performed less efficiently when isopropanol was omitted, indicating the indispensable role of the reductant in the reaction (Table 1, entry 8). Only a trace amount of product was observed when $DABCO^{\cdot}(SO_2)_2$ was applied as the sulfur dioxide surrogate (Table 1, entry 9). Reducing the amount of boronic acid to 2.0 equiv resulted in a slightly lower yield (Table 1, entry 10). Additionally, both the reaction solvent and temperature were critical for the success of this transformation (Table 1, entries 11 and 12).

Table 1. Effects of variation of reaction parameters.[a]

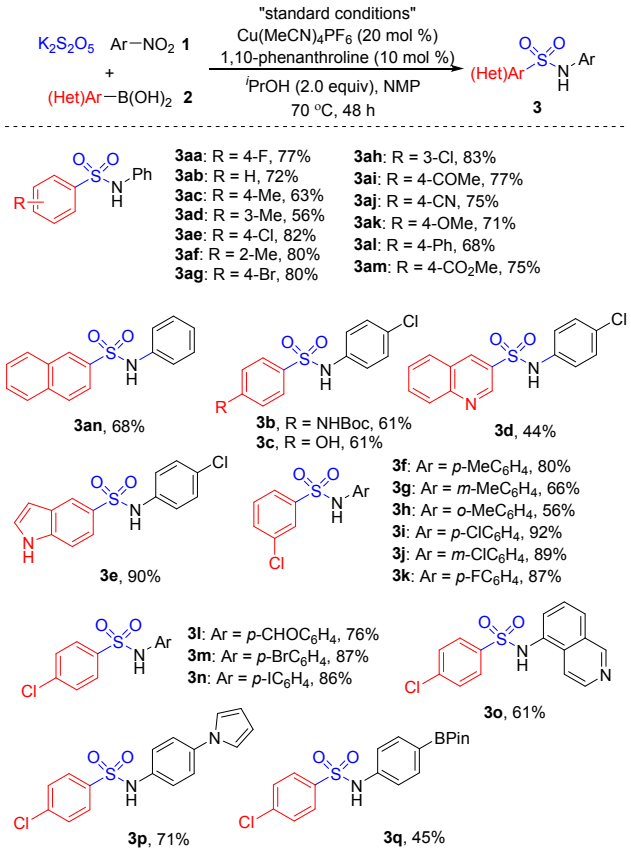


Entry	Variation from "standard conditions"	Yield (%)[b]
1	none	87 (77)
2	No $Cu(MeCN)_4PF_6$	trace
3	No 1,10-phenanthroline	46
4	20% of 1,10-phenanthroline instead of 10%	33
5	10% $Cu(MeCN)_4PF_6$ and 5% ligand	64
6	CuCl instead of $Cu(MeCN)_4PF_6$	41
7	$Cu(OTf)_2$ instead of $Cu(MeCN)_4PF_6$	63
8	No ^{i}PrOH	42
9	$DABCO^{\cdot}(SO_2)_2$ instead of $K_2S_2O_5$	trace
10	2.0 equiv $ArB(OH)_2$ instead of 3.0 equiv	71
11	DMAc instead of NMP	73
12	60 °C instead of 70 °C	49

[a] Standard conditions: nitrobenzene **1a** (0.2 mmol, 1.0 equiv), 4-fluorobenzeneboronic acid **2a** (0.6 mmol, 3.0 equiv), $K_2S_2O_5$ (0.6 mmol, 3.0 equiv), isopropanol (0.4 mmol, 2.0 equiv), $Cu(MeCN)_4PF_6$ (20 mol %), 1,10-phenanthroline (10 mol %), NMP (2.0 mL), 70 °C, 48 h. [b] ^{19}F NMR yield using 4-fluoroanisole as internal standard. Isolated yield of entry 1 is shown in parentheses.

Under the optimized conditions as above, a range of nitroarenes **1** and arylboronic acids **2** were employed in the copper-catalyzed sulfur dioxide insertion reaction. The results are showed in Table 2. It was found that the corresponding sulfonamides were afforded in good to excellent yields with broad substrate scope. Various functional groups including hydroxyl, cyano, amino, and carbonyl were all tolerated under the conditions. For example, product **3ai** was afforded in 77% yield when 4-acetylphenylboronic acid was employed. 4-Hydroxyphenylboronic acid reacted with nitrobenzene and potassium metabisulfite gave rise to the desired product **3c** in 61% yield. Boc-protected amino group and nitro-containing heterocycles were also compatible under the copper-catalyzed conditions. With regards to nitroarenes, iodo, boronic ester, aldehyde and pyrrolyl-substitutions were all susceptible during the transformation. Additionally, during our attempts to lower the catalyst loading in gram-scale synthesis, product **3i** was obtained in 73% yield with 2 mol % of $Cu(MeCN)_4PF_6$ and 1 mol % of ligand on 3.0 mmol scale (see ESI for details). However, the reaction time was prolonged to 96 h.

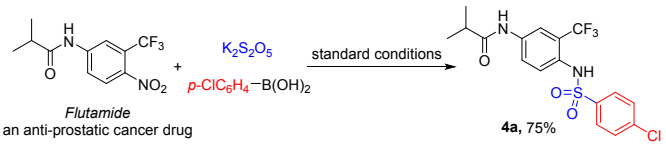
Table 2. Copper-catalyzed three-component reaction of arylboronic acids, nitroarenes, and potassium metabisulfite.[a]



[a] Isolated yield based on nitroarene **1**.

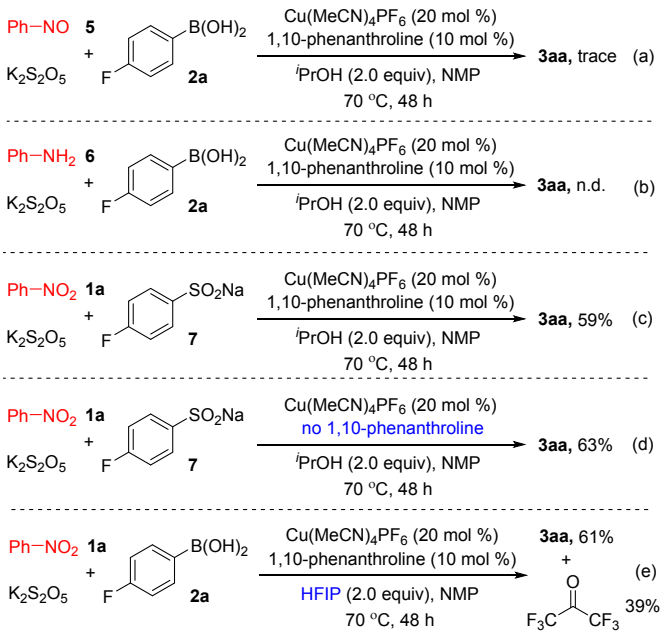
This approach was further extended to the late-stage modification of current marketed pharmaceuticals. For instance, Flutamide (an anti-prostatic cancer drug) reacted with 4-chlorophenylboronic acid and potassium metabisulfite under

the standard conditions leading to the corresponding product **4a** in 75% yield (Scheme 1).



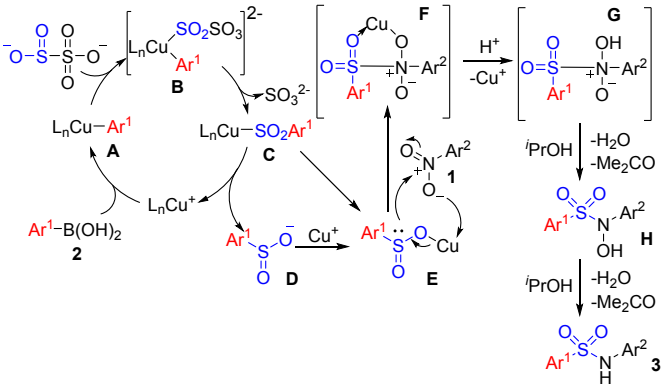
Scheme 1. Late-stage modification of Flutamide

To gain more insight into the mechanism of this reaction, several control experiments were performed as shown in Scheme 2. Only a trace amount of product **3aa** was detected when nitrosobenzene **5** was employed as a replacement of nitrobenzene **1a** in the reaction of 4-fluorobenzeneboronic acid **2a** with potassium metabisulfite under the standard conditions (Scheme 2, eq a). No reaction occurred when aniline **6** was used instead (Scheme 2, eq b). Interestingly, the reaction proceeded smoothly to afford the desired product **3aa** when 4-fluorophenylsulfinate was utilized as the substrate in the copper-catalyzed reaction with or without the addition of 1,10-phenanthroline (Scheme 2, eq c and d), indicating the unnecessity of phenanthroline ligand in the process of S-N bond construction. The reaction of nitrobenzene **1a**, 4-fluorobenzeneboronic acid **2a** and potassium metabisulfite in HFIP worked efficiently as well, giving rise to product **3aa** in 61% yield with the release of hexafluoropropan-2-one (Scheme 2, eq e). From these results, it seemed that the reaction pathway didn't include the reduction of nitrobenzene to nitrosobenzene **5** or aniline **6**.



Scheme 2. Investigation of the mechanism

On the basis of the above results and inspired by the previous reports that the S-N bond could be formed by the interaction of sulfinate species with nitro group with the assistance of transition metal,[12] a plausible mechanism was proposed in Scheme 3. At the beginning, arylboronic acid **2** would be converted into the arylsulfinate intermediate **D** by the developed copper-phenanthroline catalytic system in the presence of the sulfur dioxide surrogate (**A**-**B**-**C**-**D**).[11e,13] The successive trapping of the generated arylsulfinate **D** by free Cu(I) species and nitroarene would construct the S-N bond giving rise to the key intermediate **F**, which would be protonated to afford intermediate **G**. Subsequently, reduction of intermediate **G** by isopropanol would produce sulfonylhydroxylamine **H**, and the final product **3** would be provided by further reduction. It was found that S(VI) sulfuric species could be detected in the reaction mixture, indicating that some S(IV) species might serve as the reductant in the whole process.[11g,12] However, ^{i}PrOH was a better reductant than the S(IV) species themselves in the reaction, giving rise to a higher yield.



Scheme 3. Plausible mechanism

In conclusion, we have discovered that nitroarenes can be used as the coupling partner in the preparation of sulfonamides via the insertion of sulfur dioxide. This three-component reaction of arylboronic acids, nitroarenes, and potassium metabisulfite under copper catalysis proceeds smoothly, giving rise to a range of sulfonamides in good to excellent yields with broad substrate scope. Various functional groups including hydroxyl, cyano, amino, and carbonyl are all tolerated. A plausible mechanism is proposed, showing arylsulfinate is the intermediate and the copper-assisted interaction of nitroarene and arylsulfinate is the key step. This approach is also extended to the late-stage modification of current marketed drug (Flutamide).

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Conflicts of interest

There are no conflicts to declare.

Notes and references

1 (a) N. Ono, *The Nitro Group in Organic Synthesis*, 1st Edition; Wiley–VCH: New York, 2001. (*b*) C. Ma, F. Jiang, F.-T. Sheng, Y. Jiao, G.-J. Mei and F. Shi, *Angew. Chem. Int. Ed.* 2019, **58**, 3014; (*c*) D. Ren,

B. Liu, X. Li, S. Koniarz, M. Pawlicki, and P. J. Chmielewski, *Org. Chem. Front.*, 2019, **6**, 908.

2 For review, see: Y. Wang, Q. Ye, G. Qiu and J.-B. Liu, *Chin. J. Org. Chem.,* 2018, **38**, 1650. For selected examples: (*a*) X. Fu, Y. Meng, X. Li, M. Stepień and P. J. Chmielewski, *Chem. Commun*., 2018, **54**, 2510; (*b*) X. Li, Y. Meng, P. Yi, M. Stepień and P. J. Chmielewski, *Angew. Chem. Int. Ed.,* 2017, **56**, 10810; (*c*) B. Liu, T. Yoshida, X. Li, M. Stepień, H. Shinokubo and P. J. Chmielewski, *Angew. Chem. Int. Ed.,* 2016, **55**, 13142; (*d*) Z. Deng, X. Li, M. Stepień and P. J. Chmielewski, *Chem. Eur. J.,* 2016, **22**, 4231; (*e*) K. Deng, X. Li and H. Huang, *Electrochimica Acta*., 2016, **204**, 84; (*f*) B. Liu, X. Li, M. Stepień and P. J. Chmielewski, *Chem. Eur. J.,* 2015, **21**, 7790; (*g*) B. Liu, H. Fang, X. Li, W. Cai, L. Bao, M. Rudolf, F. Plass, L. Fan, X. Lu and D. M. Guldi, *Chem. Eur. J.,* 2015, **21**, 746; (*h*) B. Liu, X. Li, J. Maciołek, M. Stepień and P. J. Chmielewski, *J. Org. Chem.,* 2014, **79**, 3129; (*i*) B. Liu, X. Li, X. Xu, M. Stepień and P. J. Chmielewski, *J. Org. Chem.,* 2013, **78**, 1354; (*j*) X. Li, B. Liu, P. J. Chmielewski and X. Xu, *J. Org. Chem.,* 2012, **77**, 8206; (*k*) X. Li, B. Liu, X. Yu, P. Yi, R. Yi and P. J. Chmielewski, *J. Org. Chem.,* 2012, **77**, 2431; (*l*) X. Li, B. Liu, P. Yi, R. Yi, X. Yu and P. J. Chmielewski, *J. Org. Chem.,* 2011, **76**, 2345.

3 (*a*) X. Zheng, J. Ding, J. Chen, W. Gao, M. Liu and H. Wu, *Org. Lett.,* 2011, **13**, 1726; (*b*) J. Zhang, J. Chen, M. Liu, X. Zheng, J. Ding and H. Wu, *Green Chem.,* 2012, **14**, 912.

4 (*a*) M. R. Yadav, M. Nagaoka, M. Kashihara, R.-L. Zhong, T. Miyazaki, S. Sakaki and Y. Nakao, *J. Am. Chem. Soc.,* 2017, **139**, 9423; (*b*) M. Kashihara, M. R. Yadav and Y. Nakao, *Org. Lett.,* 2018, **20**, 1655; (*c*) F. Inoue, M. Kashihara, M. R. Yadav and Y. Nakao, *Angew. Chem., Int. Ed.* 2017, **56**, 13307; (*d*) R.-L. Zhong, M. Nagaoka, Y. Nakao and S. Sakaki, *Organometallics* 2018, **37**, 3480.

5 W. Chen, K. Chen, W. Chen, M. Liu and H. Wu, *ACS Catal.,* 2019, **9**, 8110.

6 P. S. Santos and M. T. S. Mello, *J. Mol. Struc.,* 1988, **178**, 121.

7 For selected examples, see: (*a*) B. Nguyen, E. J. Emmet and M. C. Willis, *J. Am. Chem. Soc.,* 2010, **132**, 16372; (*b*) J. Zhang, M. Yang, J.-B. Liu, F.-S. He and J. Wu, *Chem. Commun.* 2020, DOI: 10.1039/D0CC00375A; (*c*) X. Gong, M. Yang, J.-B. Liu, F.-S. He, X. Fan and J. Wu, *Green Chem.* 2020, DOI: 10.1039/D0GC00332H; (*d*) K. Zhou, J.-B. Liu, W. Xie, S. Ye and J. Wu, *Chem. Commun.* 2020, DOI: 10.1039/D0CC00351D; (*e*) X. Gong, M. Wang, S. Ye and J. Wu, *Org. Lett.,* 2019, **21**, 1156; (*f*) S. Ye, G. Qiu and J. Wu, *Chem. Commun.,* 2019, **55**, 1013; (*g*) S. Ye, D. Zheng, J. Wu and G. Qiu, *Chem. Commun.,* 2019, **55**, 2214; (*h*) S. Ye, Y. Li, J. Wu and Z. Li, *Chem. Commun.,* 2019, **55**, 2489; (*i*) X. Gong, X. Li, W. Xie, J. Wu and S. Ye, *Org. Chem. Front.,* 2019, **6**, 1863; (*j*) S. Ye, T. Xiang, X. Li and J. Wu, *Org. Chem. Front.,* 2019, **6**, 2183; (*k*) J. Zhang, W. Xie, S. Ye and J. Wu, *Org. Chem. Front.,* 2019, **6**, 2254; (*l*) F.-S. He, X. Gong, P. Rojsitthisak and J. Wu, *J. Org. Chem.,* 2019, **84**, 13159; (*m*) S. Ye, X. Li, W. Xie and J. Wu, *Asian J. Org. Chem.,* 2019, **8**, 893; (*n*) S. Ye, K. Zhou, P. Rojsitthisak and J. Wu, *Org. Chem. Front.,* 2020, **7**, 14. (*o*) S. Ye and J. Wu, *Acta Chim. Sinica,* 2019, **77**, 814.

8 For selected reviews, see: (*a*) G. Qiu, K. Zhou, L. Gao and J. Wu, *Org. Chem. Front.,* 2018, **5**, 691; (*b*) K. Hofman, N. Liu and G. Manolikakes, *Chem. Eur. J.,* 2018, **24**, 11852; (*c*) G. Liu, C. Fan and J. Wu, *Org. Biomol. Chem.,* 2015, **13**, 1592; (*d*) G. Qiu, L. Lai, J. Cheng and J. Wu, *Chem. Commun.,* 2018, **54**, 10405; (*e*) Qiu, K. Zhou and J. Wu, *Chem. Commun.,* 2018, **54**, 12561; (*f*) A. S. Deeming, E. J. Emmett, C. S. Richards-Taylor and M. C. Willis, *Synthesis* 2014, **46**, 2701; (*g*) P. Bisseret and N. Blanchard, *Org. Biomol. Chem.,* 2013, **11**, 5393; (*h*) S. Ye, G. Qiu and J. Wu, *Chem. Commun.,* **2019**, *55*, 1013. For selected examples, see: For recent selected examples, see: (*a*) Z. Chen, N.-W. Liu, M. Bolte, H. Ren and G. Manolikakes, *Green Chem.*, 2018, **20**, 3059; (*b*) Q. Lin, Y. Liu, Z. Xiao, L. Zheng, X. Zhou, Y. Guo, Q.-Y. Chen, C. Zheng and C. Liu, *Org. Chem. Front.*, 2019, **6**, 447; (*c*) X. Y. Qin, L. He, J. Li, W. J. Hao, S. J. Tu and B. Jiang, *Chem. Commun.*, 2019, **55**, 3227; (*d*) R. J. Reddy, A. H. Kumari, J. J. Kumar and J. B. Nanubolu, *Adv. Synth. Catal.*, 2019, **361**, 1587; (*e*) L. Lu, C. Luo, H. Peng, H. Jiang, M. Lei and B. Yin, *Org. Lett.*, 2019, **21**, 2602.

9 (*a*) Y.-C. Wang, R.-X. Wang, G. Qiu, H. Zhou, W. Xie and J.-B. Liu, *Org. Chem. Front.*, 2019, **6**, 2471; (*b*) R. Liu, M. Li, W. Xie, H. Zhou, Y. Zhang and G. Qiu, *J. Org. Chem*. 2019, **84**, 11763; (*c*) Y.-C. Wang, J.-B. Liu, H. Zhou, W. Xie, P. Rojsitthisak and G. Qiu, *J. Org. Chem.* 2020, DOI:10.1021/acs.joc.9b02590; (*d*) W. Xie, Y. Wu, J. Zhang, Q. Mei, Y. Zhang, N. Zhu, Q. Liu and H. Zhang, *Eur. J. Med. Chem.,* 2018, **145**, 35; (*e*) W. Xie, S. Xie, Y. Zhou, X. Tang, J. Liu, W. Yang and M. Qiu, *Eur. J. Med. Chem.,* 2014, **81**, 22; (*f*) W. Xie, H. Zhang, J. He, J. Zhang, Q. Yu, C. Luo and S. Li, *Bioorg. Med. Chem. Lett.,* 2017, **27**, 530; (*g*) Y. Zheng, M. Liu, G. Qiu, W. Xie and J. Wu, *Tetrahedron,* 2019, **75**, 1663; (*h*) L. X. Gong, J. Chen, X. Li, W. Xie and J. Wu, *Chem. Asian J.* 2018, **13**, 2543; (*i*) C. Ma, J.-Y. Zhou, Y.-Z. Zhang, Y. Jiao, G.-J. Mei and F. Shi, *Chem. Asian J.* 2018, **13**, 2549; (*j*) S. Qiu, C. Wang, S. Xie, X. Huang, L. Chen, Y. Zhao and Z. Zeng, *Chem. Commun.,* 2018, **54**, 11383; (*k*) T. Guo, X.-N. Wei, Y. Liu, P.-K. Zhang and Y.-H. Zhao, *Org. Chem. Front.,* 2019, **6**, 1414.

10 For selected examples, see: (*a*) Y. Zong, L. Lang, M. Yang, X. Li, X. Fan and J. Wu, *Org. Lett.,* 2019, **21**, 1935; (*b*) J. Zhang, X. Li, W. Xie, J. Wu and S. Ye, *Org. Lett.,* 2019, **21**, 4950; (*c*) X. Wang, M. Yang, W. Xie, X. Fan and J. Wu, *Chem. Commun.,* 2019, **55**, 6010; (*d*) F.-S. He, Y. Wu, X. Li, H. Xia and J. Wu, *Org. Chem. Front.,* 2019, **6**, 1873; (*e*) H. Tang, Y. Kuang, J. Zeng, X. Li, W. Zhou and Y. Lu, *RSC Adv.* 2019, **9**, 31474; (*f*) S. Ye, X. Li, W. Xie and J. Wu, *Eur. J. Org. Chem.* 2020, **15**, 10.1002/ejoc.201900396; (*g*) X. Wang, Y. Kuang, S. Ye and J. Wu, *Chem. Commun.,* 2019, **55**, 14962.

11 (*a*) S. Ye and J. Wu, *Chem. Commun.,* 2012, **48**, 7753; (*b*) S. Ye and J. Wu, *Chem. Commun.,* 2012, **48**, 10037; (*c*) T. Liu, D. Zheng, Z. Li and J. Wu, *Adv. Synth. Catal.,* 2017, **359**, 2653; (*d*) F. Zhang, D. Zheng, L. Lai, J. Cheng, J. Sun and J. Wu, *Org. Lett.,* 2018, **20**, 1167; (*e*) Y. Chen, P. R. D. Murray, A. T. Davies and M. C. Willis, *J. Am. Chem. Soc.,* 2018, **140**, 8781; (*f*) M. Wang, Q. Fan and X. Jiang, *Green Chem.,* 2018, **20**, 5469; (*g*) X. Marset, J. Torregrosa-Crespo, R. M. Martinez-Espinosa, G. Guillena and D. J. Ramón, *Green Chem.,* 2019, **21**, 4127.

12 W. Zhang, J. Xie, B. Rao and M. Luo, *J. Org. Chem.,* 2015, **80**, 3504.

13 Y. Chen and M. C. Willis, *Chem. Sci.,* 2017, **8**, 3249.

Copper-catalyzed synthesis of sulfonamides from nitroarenes with the insertion of sulfur dioxide

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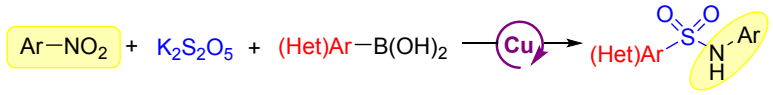
Graphical Abstract



up to 97% yield

- *synthesis of sulfonamides from nitroarenes*
- *copper-catalyzed three-cmponent reaction*
- *insertion of sulfur dioxide*

A three-component reaction of arylboronic acids, nitroarenes, and potassium metabisulfite under copper catalysis proceeds smoothly, giving rise to a range of sulfonamides in good to excellent yields with broad substrate scope. This approach is also extended to the late-stage modification of current marketed drug (Flutamide).